IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of
Motonori MIYAKAWA, et al.
Serial No. 10/522,553 Art Unit: 1625
Filed: August 1, 2003 Examiner: Rita J. Desai
For: NOVEL TETRAHYDROQUINOLINE DERIVATIVES

D E C L A R A T I O N

Commissioner for Patents
P.O.Box 1450
Alexandria, VA 22313-1450

Sir:

I, Kazuyuki Furuya, a Japanese citizen, residing at 123-6, Katsu-cho, Nagahama, Shiga, Japan, do hereby solemnly and sincerely declare that:

I graduated from Kyoto Institute of Technology, department of applied biology and obtained a master's degree from the same University in 1995;

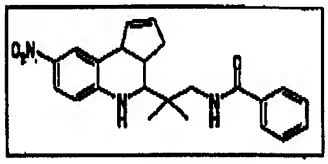
I am working for Kaken Pharmaceutical Co., Ltd., the Assignee of the above-identified application, for 2 years in the pharmacological research department and later in the drug discovery department;

I obtained a young investigator award in the American Society for Bone and Mineral Research;

I am one of the co-inventors of the above-identified application and am familiar with the disclosure and the claims of said application; and

In order to compare an androgen receptor agonistic action of the claimed compounds of the above-identified application with the compounds disclosed in WO 01/27086, I conducted the following experiment to determine the androgen receptor agonistic action of the compound disclosed in WO 01/27086 which is structurally the closest to the claimed compounds of the above-identified application.

A test compound is the compound of Example 56 in WO 01/27086, represented by the following formula:



Testes were removed from 12-week-old male SD rats. From the following day onward, the compound of Example 56 in WO 01/27086 (60 mg/kg) was subcutaneously administered once daily for 4 consecutive weeks on 5 days per week. The compound of WO 01/27086 was dissolved in dimethyl sulfoxide, and then diluted 10-fold with olive oil. The resulting solution of each concentration was used in the test. In an ORX control group, dimethyl sulfoxide diluted 10-fold with olive oil was used for the test. The rats, which had not been orchiectomized, but had undergone laparotomy, followed by closure of the abdomen, were used as a sham control group. On the next day after final administration, the wet weights of the ventral prostate and the levator ani muscle were measured, and the bone mineral density of the right femur

was measured by the DEXA method (dual energy X-ray absorptiometry), to evaluate the *in vivo* effect of the compounds. The results are shown in the Attachment. They show that the compound of Example 56 in WO 01/27086 did not show a significant androgen receptor agonistic action on bone mineral density even in an amount of 60 mg/kg.

The undersigned declarant declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed this 2nd day of November, 2007.

古屋 和行

Kazuyuki Furuya

*: P<0.05 vs ORX Vehicle
**: P<0.01 vs ORX Vehicle